

9/678, 851  
(FILE 'HOME' ENTERED AT 11:03:46 ON 23 JUN 2003)

FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS' ENTERED AT 11:03:58 ON 23 JUN 2003

L1 24 S GRYPHON  
L2 21 DUP REM L1 (3 DUPLICATES REMOVED)  
L3 600 S (OFFORD, R? OR OFFORD R?)/AU,IN  
L4 11124 S (THOMPSON, D? OR THOMPOSON D?)/AU,IN  
L5 358 S (WILKEN, J? OR WILKEN J?)/AU,IN  
L6 12021 S L3 OR L4 OR L5  
L7 157 S L6 AND (RANTES OR CHEMOKIN?)  
L8 0 S L7 AND ACETYLAT?  
L9 0 S L7 AND ACYLAT?  
L10 75 S L7 AND (DERIVATIV? OR ANALOG? OR VARIANT? OR N-TERMIN?)  
L11 3 S L10 AND HOMOLOG?  
L12 3 DUP REM L11 (0 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 11:07:28 ON 23 JUN 2003

FILE 'MEDLINE, WPIDS' ENTERED AT 11:09:24 ON 23 JUN 2003

FILE 'STNGUIDE' ENTERED AT 11:09:26 ON 23 JUN 2003

L13 0 S (CHEMOKIN? OR RANTES) (10A) (HEXANOYL OR ALKANOYL? OR NONANOYL?)  
L14 0 S (CHEMOKIN? OR RANTES) AND (HEXANOYL OR ALKANOYL? OR NONANOYL?)

FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS' ENTERED AT 11:11:15 ON 23 JUN 2003

L15 56 S (CHEMOKIN? OR RANTES) AND (HEXANOYL OR ALKANOYL? OR NONANOYL?)  
L16 42 DUP REM L15 (14 DUPLICATES REMOVED)  
L17 17 S (CHEMOKIN? OR RANTES) (20A) (HEXANOYL OR ALKANOYL? OR NONANOYL?)  
L18 11 DUP REM L17 (6 DUPLICATES REMOVED)  
L19 185 S (CHEMOKIN? OR RANTES) (20A) (ACETYL? OR N-ACETYL?)  
L20 3 S L19 AND ALKYLAT?  
L21 0 S L19 AND (NONANOYL? OR DECANOYL? OR OCTANOYL?)  
L22 24 S (CHEMOKINE? OR RANTES?) AND (NONANOYL? OR DECANOYL? OR OCTANOYL?)  
L23 13 DUP REM L22 (11 DUPLICATES REMOVED)

=>

12 ANSWER 3 OF 3 MEDLINE  
AN 1999214286 MEDLINE  
DN 99214286 PubMed ID: 10196243  
TI Highly potent **RANTES analogues** either prevent  
CCR5-using human immunodeficiency virus type 1 infection in vivo or  
rapidly select for CXCR4-using **variants**.  
AU Mosier D E; Picchio G R; Gulizia R J; Sabbe R; Poignard P; Picard L;  
**Offord R E; Thompson D A; Wilken J**  
CS Department of Immunology-IMM7, The Scripps Research Institute, La Jolla,  
California 92037, USA.. dmosier@scripps.edu  
NC AI29182 (NIAID)  
MO1 RR00833 (NCRR)  
SO JOURNAL OF VIROLOGY, (1999 May) 73 (5) 3544-50.  
Journal code: 0113724. ISSN: 0022-538X.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; AIDS  
EM 199905  
ED Entered STN: 19990601  
Last Updated on STN: 19990601  
Entered Medline: 19990519  
AB The natural ligands for the CCR5 **chemokine** receptor, macrophage  
inflammatory protein 1alpha (MIP-1alpha), MIP-1beta, and **RANTES**  
(regulated on T-cell activation, normal T-cell expressed and secreted),  
are known to inhibit human immunodeficiency virus (HIV) entry, and  
**N-terminally modified RANTES analogues**  
are more potent than native **RANTES** in blocking infection.  
However, potent CCR5 blocking agents may select for HIV-1 **variants**  
that use alternative coreceptors at less than fully inhibitory  
concentrations. In this study, two **N-terminal**  
chemical modifications of **RANTES** produced by total synthesis,  
aminoxyypentane (AOP)-**RANTES**[2-68] and N-nonanoyl (NNY)-  
**RANTES**[2-68], were tested for their ability to prevent HIV-1  
infection and to select for coreceptor switch **variants** in the  
human peripheral blood lymphocyte-SCID mouse model. Mice were infected  
with a CCR5-using HIV-1 isolate that requires only one or two amino acid  
substitutions to use CXCR4 as a coreceptor. Even though it achieved lower  
circulating concentrations than AOP-**RANTES** (75 to 96 pM as  
opposed to 460 pM under our experimental conditions), NNY-**RANTES**  
was more effective in preventing HIV-1 infection. However, in a subset of  
treated mice, these levels of NNY-**RANTES** rapidly selected  
viruses with mutations in the V3 loop of envelope that altered coreceptor  
usage. These results reinforce the case for using agents that block all  
significant HIV-1 coreceptors for effective therapy.

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**WEST Search History**

DATE: Monday, June 23, 2003

**Set Name Query**  
side by side**Hit Count Set Name**  
result set*DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR*

L14	L13 and (chemokin\$ or RANTES)	8	L14
L13	L12 and l11	18	L13
L12	(offord or thompson or wilken)	102679	L12
L11	gryphon	111	L11
L10	L9 and acetylats	6	L10
L9	(chemokin\$ or RANTES)near10 (N-termin\$)near20(analog\$ or derivativ\$ or variant\$)	25	L9
L8	(chemokin\$ or RANTES)near10 (N-termin!!!)near20(analog!!! or derivativ!!! or variant\$)	0	L8
L7	chemokin\$ near10 (N-termin\$)near30 (acylate!! or acylation!! or alkylat!!!)	0	L7
L6	chemokin\$ near30 (acylat\$ or alkyl\$)	43	L6
L5	chemokin\$ near30 (N-alkyl)	0	L5
L4	chemokin\$ near30 (nonanoyl or pentanoyl or hexanoyl or decanoyl)	0	L4
L3	RANTES near30 (nonanoyl or pentanoyl or hexanoyl or decanoyl)	2	L3
L2	L1 and (nonanoyl or pentanoyl or hexanoyl or decanoyl)	31	L2
L1	(inflamm\$) and RANTES	1342	L1

END OF SEARCH HISTORY